

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

Claim 1. (Currently Amended) A method of diagnosing multiple sclerosis in a subject, the method comprising

providing a test sample from a subject;

detecting in said test sample ~~at least one antibody selected from the group consisting of an anti-Glc ( $\alpha$ ) antibody, an anti-Glc ( $\alpha$  1-4) Glc ( $\alpha$ ) antibody, an anti-Glc ( $\alpha$  1-4) Glc ( $\beta$ ) antibody, an anti-Glc ( $\beta$ ) antibody, an anti-Gal ( $\beta$ ) antibody, an anti-Glc ( $\beta$  1-4) Glc ( $\beta$  1-4) Glc ( $\beta$ ) antibody, an anti-GlcNAc ( $\beta$  1-4) GlcNAc ( $\beta$ ) antibody, an anti-L-Araf ( $\alpha$ ) antibody, an anti-L-Rha ( $\alpha$ ) antibody, an anti-Gal ( $\beta$  1-3) [GlcNAc ( $\beta$  1-6)] GalNAc ( $\alpha$ ) antibody, an anti-Gal ( $\beta$  1-4) GlcNAc ( $\alpha$ ) antibody, an anti-Gal ( $\beta$  1-3) GalNAc ( $\alpha$ ) antibody, an anti-Gal ( $\beta$  1-3) GlcNAc ( $\beta$ ) antibody, an anti-GlcA ( $\beta$ ) antibody, an anti-GlcA ( $\beta$ ) antibody, and an anti-Xyl ( $\alpha$ ) antibody; and~~

comparing the levels of said ~~at least one~~ antibody in said test sample to the levels of said ~~at least one~~ antibody in a control sample, wherein said control sample is selected from the group consisting of one or more individuals that have multiple sclerosis symptoms and have a known multiple sclerosis status, and one or more individuals that do not show multiple sclerosis symptoms,

thereby diagnosing multiple sclerosis in said subject.

Claim 2. (Currently Amended) The method of claim 1, wherein said method further comprises

detecting a second antibody selected from the group consisting of an anti-Glc ( $\alpha$ ) antibody, an anti-Glc ( $\alpha$  1-4) Glc ( $\beta$ ) antibody, an anti-Glc ( $\beta$ ) antibody, an anti-Gal ( $\beta$ ) antibody, an anti-Glc ( $\beta$  1-4) Glc ( $\beta$  1-4) Glc ( $\beta$ ) antibody, an anti-GlcNAc ( $\beta$  1-4) GlcNAc ( $\beta$ ) antibody, an anti-L-Araf ( $\alpha$ ) antibody, an anti-L-Rha ( $\alpha$ ) antibody, an anti-GlcNAc( $\alpha$ ) antibody, an anti-Gal ( $\beta$  1-3) [GlcNAc ( $\beta$  1-6)] GalNAc ( $\alpha$ ) antibody, an anti-Gal ( $\beta$  1-4) GlcNAc ( $\alpha$ ) antibody, an anti-Gal ( $\beta$  1-3) GalNAc ( $\alpha$ ) antibody, an anti-Gal ( $\beta$  1-3) GlcNAc ( $\beta$ ) antibody,

an anti-GlcA ( $\alpha$ ) antibody, an anti-GlcA ( $\beta$ ) antibody, and an anti-Xyl ( $\alpha$ ) antibody ~~an anti-Glc ( $\alpha$ ) antibody in said test sample; and~~

comparing the levels of the second antibody in said test sample to the levels of the second antibody in a control sample, wherein said control sample is selected from the group consisting of one or more individuals that have multiple sclerosis symptoms and have a known multiple sclerosis status, and one or more individuals that do not show multiple sclerosis symptoms ~~said antibody in said test sample to said control sample;~~

thereby diagnosing multiple sclerosis in said subject.

Claim 3. (Currently Amended) The method of claim 2, wherein the second antibody is an anti-Glc ( $\alpha$ ) antibody ~~said method comprises detecting an anti-Glc ( $\alpha$  1-4) Glc ( $\alpha$ ) antibody in said test sample; and comparing the levels of said antibodies in said test sample to said control sample.~~

Claim 4. (Currently Amended) The method of claim 1, wherein said control sample consists essentially of a population of one or more individuals that do not show multiple sclerosis symptoms ~~method comprises detecting an anti-Glc ( $\alpha$  1-4) Glc ( $\alpha$ ) antibody and an anti-Glc ( $\alpha$ ) antibody in said test sample; and comparing the level of said antibodies in said test sample to said control sample.~~

Claim 5. (Previously Presented) The method of claim 1, wherein said control sample consists essentially of a population of one or more individuals that have multiple sclerosis symptoms with a known multiple sclerosis status.

Claim 6. (Previously Presented) The method of claim 1, wherein said test sample is a biological fluid.

Claim 7. (Previously Presented) The method of claim 6, wherein said biological fluid is whole blood, serum, plasma, spinal cord fluid, urine, or saliva.

Claim 8. (Previously Presented) The method of claim 1, wherein said biological fluid is serum.

Claim 9. (Previously Presented) The method of claim 1, wherein said subject is a female.

Claim 10. (Previously Presented) The method of claim 1, wherein said subject is a male.

Claim 11. (Previously Presented) The method of claim 1, wherein said at least one antibody is an IgM type antibody.

Claim 12. (Previously Presented) The method of claim 1, wherein said at least one antibody is an IgA type antibody.

Claim 13. (Previously Presented) The method of claim 1, wherein said at least one antibody is an IgG type antibody.

Claim 14. (Previously Presented) The method of claim 2, wherein said anti-Glc ( $\alpha$ ) antibody is an IgM type antibody.

Claim 15. (Previously Presented) The method of claim 3, wherein said anti-Glc ( $\alpha$  1-4) Glc ( $\alpha$ ) antibody is an IgM type antibody.

Claim 16. (Previously Presented) The method of claim 1, wherein said diagnosis is an early diagnosis of multiple sclerosis.

Claim 17. (Previously Presented) The method of claim 1, wherein said control sample is determined using an Expanded Disability Status Scale (EDSS) assessment or a Magnetic Resonance Imaging (MRI) assessment.

Claim 18. (Previously Presented) The method of claim 1, wherein said control sample is determined using an Expanded Disability Status Scale (EDSS) assessment.

Claim 19. (Previously Presented) The method of claim 1, wherein said method comprises detecting at least two of said antibodies.

Claim 20. (Previously Presented) The method of claim 1, wherein said method comprises detecting at least four of said antibodies.

Claim 21. (Previously Presented) The method of claim 1, wherein said method comprises detecting at least six of said antibodies.

Claim 22. (Currently Amended) A method of diagnosing a multiple sclerosis exacerbation in a subject, the method comprising

providing a test sample from a subject;

detecting ~~an anti-Glc ( $\alpha$ ) IgM type antibody or an anti-Glc ( $\alpha$  1-4) Glc ( $\alpha$ ) IgM type antibody~~ in said test sample; and

comparing the levels of said antibody in said test sample to a control sample, wherein said control sample is derived from one or more individuals whose multiple sclerosis status is known,

thereby diagnosing multiple sclerosis exacerbation in said subject.

Claim 23. (Currently Amended) The method of claim 22, wherein said control sample consists essentially of a population of one or more individuals that have multiple sclerosis symptoms with a known multiple sclerosis status ~~method comprises detecting an anti-Glc ( $\alpha$ ) IgM type antibody in said test sample; and comparing the levels of said antibody in said test sample to said control sample.~~

Claim 24. (Currently Amended) The method of claim 22, wherein said method comprises detecting an anti-Glc ( $\alpha$  1-4) Glc ( $\alpha$ )  ~~$\alpha$~~  IgM type antibody and an anti-Glc ( $\alpha$ ) IgM type antibody in said test sample; and

comparing the levels of said antibody in said test sample to said control sample.

Claim 25. (Currently Amended) The method of claim 22, wherein said method comprises detecting an anti- $\alpha$ -Glucose IgM type antibody and an anti-Glc ( $\alpha$  1-4) Glc ( $\alpha$ )  $\alpha$  IgM type antibody in said test sample; and comparing the levels of said antibodies in said test sample to said control sample.

Claim 26. (Previously Presented) The method of claim 22, wherein said control sample consists essentially of a population of one or more individuals in remission multiple sclerosis status that do not show symptoms of a multiple sclerosis exacerbation, and a multiple sclerosis exacerbation is diagnosed in said subject if more anti-Glc ( $\alpha$ ) antibody or anti-Glc ( $\alpha$  1-4) Glc ( $\alpha$ ) antibody is present in said test sample than in said control sample.

Claim 27. (Previously Presented) The method of claim 22, wherein said control sample consists essentially of a population of one or more individuals that their multiple sclerosis status in exacerbation, and show symptoms of a multiple sclerosis exacerbation, and a multiple sclerosis exacerbation is diagnosed in said subject if similar anti-Glc ( $\alpha$ ) antibody or anti-Glc ( $\alpha$  1-4) Glc ( $\alpha$ ) antibody levels is present in said test sample and in said control sample.

Claim 28. (Previously Presented) The method of claim 22, wherein said test sample is a biological fluid.

Claim 29. (Previously Presented) The method of claim 28, wherein said biological fluid is whole blood, serum, plasma, spinal cord fluid, urine, or saliva.

Claim 30. (Previously Presented) The method of claim 28, wherein said biological fluid is serum.

Claim 31. (Previously Presented) The method of claim 22, wherein said subject is a female.

Claim 32. (Previously Presented) The method of claim 22, wherein said subject is a male.

Claim 33. (Previously Presented) The method of claim 22, wherein said diagnosis is an early diagnosis of multiple sclerosis exacerbation.

Claim 34. (Previously Presented) The method of claim 22, wherein said subject has been treated by subcutaneous administration of interferon beta.

Claim 35. (Previously Presented) The method of claim 22, wherein said subject has been treated by subcutaneous administration of glitamerer acetate.

Claim 36. (Currently Amended) A method for assessing multiple sclerosis disease severity in a subject, the method comprising

providing a test sample from a subject;

determining whether said test sample contains ~~an anti- $\alpha$ -Glucose IgM type antibody~~ or an anti-Glc ( $\alpha$  1-4) Glc ( $\alpha$ ) IgM type antibody; and

comparing the level of said at least one antibody in said test sample to a control sample, wherein said control sample is derived from one or more individuals whose multiple sclerosis disease severity is known.

thereby assessing of multiple sclerosis severity in said subject.

Claim 37. (Currently Amended) The method of claim 36, wherein said control sample consists essentially of a population of one or more individuals that have multiple sclerosis symptoms with a known multiple sclerosis status ~~method comprises detecting an anti-Glc ( $\alpha$ ) IgM type antibody in said test sample; and comparing the levels of said antibody in said test sample to said control sample.~~

Claim 38. (Currently Amended) The method of claim ~~36~~ 35, wherein said method comprises detecting an anti-Glc ( $\alpha$  1-4) Glc ( $\alpha$ ) IgM type antibody and an anti-Glc ( $\alpha$ ) IgM type antibody in said test sample; and comparing the levels of said antibodies in said test sample to said control sample.

Claim 39. (Currently Amended) The method of claim ~~37~~ 35, wherein said method comprises

detecting an anti-Glc ( $\alpha$  1-4) Glc ( $\alpha$ ) IgM type antibody and an anti-Glc ( $\alpha$ ) IgM type antibody in said test sample; and

comparing the level of said antibodies in said test sample to said control sample.

Claim 40. (Previously Presented) The method of claim 36, wherein said control sample consists essentially of a population of one or more individuals whose multiple sclerosis disease severity is defined by Expanded Disability Status Scale (EDSS), changes in an EDSS score, or a Magnetic Resonance Imaging (MRI) assessment.

Claim 41. (Previously Presented) The method of claim 36, wherein said test sample is a biological fluid.

Claim 42. (Previously Presented) The method of claim 41, wherein said biological fluid is whole blood, serum, plasma, spinal cord fluid, urine, saliva.

Claim 43. (Previously Presented) The method of claim 41, wherein said biological fluid is serum.

Claim 44. (Previously Presented) The method of claim 36, wherein said subject is a female.

Claim 45. (Previously Presented) The method of claim 36, wherein said subject is a male.

Claim 46. (Currently Amended) The method of claim 36, further comprising selecting a therapeutic agent for treating multiple sclerosis, the method comprising  
determining whether said test sample contains anti  $\alpha$ -Glucose  $\alpha$  antibody ; and  
selecting a therapeutic agent and dosage regimen based on the relative levels of said antibody in said subject sample and said control sample.

Claim 47. (Previously Presented) The method of claim 46, wherein said method further comprises

determining whether said test sample contains an anti-Glc ( $\alpha$  1-4) Glc ( $\alpha$ ) antibody; and

comparing the levels of said an anti-Glc ( $\alpha$  1-4) Glc ( $\alpha$ ) antibody in said test sample to levels of antibody in a control sample consisting essentially of one or more individuals whose multiple sclerosis status is known.

Claim 48. (Currently Amended) A kit for diagnosing symptoms associated with multiple sclerosis, the kit comprising:

a first glycan reagent that specifically detects an anti-Glc ( $\alpha$  1-4) Glc ( $\alpha$ ) antibody;

a second glycan reagent that specifically detects a second antibody selected from the group consisting of an anti-Glc ( $\alpha$ ) antibody, an anti-Glc ( $\alpha$  1-4) Glc ( $\beta$ ) antibody, an anti-Glc ( $\beta$ ) antibody, an anti-Gal ( $\beta$ ) antibody; an anti-Glc ( $\beta$  1-4) Glc ( $\beta$  1-4) Glc ( $\beta$ ) antibody, an anti-GlcNAc ( $\beta$  1-4) GlcNAc ( $\beta$ ) antibody, an anti-L-Araf ( $\alpha$ ) antibody, an anti-L-Rha ( $\alpha$ ) antibody, an anti-GlcNAc( $\alpha$ ) antibody, an anti-Gal ( $\beta$ 1-3) [GlcNAc ( $\beta$ 1-6)] GalNAc ( $\alpha$ )antibody, an anti-Gal ( $\beta$  1-4) GlcNAc ( $\alpha$ )antibody, an anti-Gal ( $\beta$  1-3) GalNAc ( $\alpha$ ) antibody, an anti-Gal ( $\beta$  1-3) GlcNAc ( $\beta$ ) antibody, an anti-GlcA ( $\alpha$ ) antibody, an anti-GlcA ( $\beta$ ) antibody, and an anti-Xyl ( $\alpha$ ) antibody ~~an anti-Glc ( $\alpha$  1-4) Glc ( $\alpha$ ) antibody;~~ and  
directions for using said kit.

Claim 49. (Previously Presented) The kit of claim 48, further comprising a reagent that specifically detects an IgM type antibody.

Claim 50. (New) A substrate comprising a reagent that detects an antibody specific for Glc( $\alpha$  1-4) Glc ( $\alpha$ ) .

Claim 51. (New) The substrate of claim 50, further comprising a reagent that detects an antibody selected from the group consisting of an anti-Glc ( $\alpha$  1-4) Glc ( $\alpha$ ) antibody, an anti-Glc ( $\alpha$  1-4) Glc ( $\beta$ ) antibody, an anti-Glc ( $\beta$ ) antibody, an anti-Gal ( $\beta$ ) antibody; an anti-Glc ( $\beta$  1-4) Glc ( $\beta$  1-4) Glc ( $\beta$ )antibody, an anti-GlcNAc ( $\beta$  1-4) GlcNAc ( $\beta$ )antibody, an anti-L-Araf ( $\alpha$ ) antibody, an anti-L-Rha ( $\alpha$ )antibody, an anti-GlcNAc( $\alpha$ ) antibody, an anti-Gal ( $\beta$ 1-3) [GlcNAc ( $\beta$ 1-6)] GalNAc ( $\alpha$ ) antibody, an anti-Gal ( $\beta$  1-4) GlcNAc ( $\alpha$ ) antibody, anti-Glc ( $\alpha$ ) antibody,



an anti-Gal ( $\beta$  1-3) GalNAc ( $\alpha$ ), an anti-Gal ( $\beta$  1-3) GlcNAc ( $\beta$ ), an anti-GlcA ( $\alpha$ ) antibody, or an anti-GlcA ( $\beta$ ) antibody, and an anti-Xyl ( $\alpha$ ) antibody.

Claim 52. (New) The substrate of claim 50, further comprising a reagent that detects an anti-Glc ( $\alpha$ ) antibody.

Claim 53. (New) The substrate of claim 50, further comprising a reagent that detects an anti-L-Rha ( $\alpha$ ) antibody.

Claim 54. (New) The substrate of claim 52, further comprising a reagent that detects an anti-L-Rha ( $\alpha$ ) antibody.

Claim 55. (New) The substrate of claim 50, further comprising a reagent that detects an anti-GlcNAc( $\alpha$ ) antibody.

Claim 56. (New) The substrate of claim 52, further comprising a reagent that detects an anti-GlcNAc( $\alpha$ ) antibody.

Claim 57. (New) The substrate of claim 50, wherein said substrate is planar.

Claim 58. (New) The substrate of claim 50, wherein said substrate is provided as a well of a micro-titer plate.

Claim 59. (New) The substrate of claim 50, wherein said reagent is a monosaccharide or oligosaccharide.